layer of lesser density, whereby the gradient has been prepared in a 15 mL conical tube in a total liquid volume of not less than 5 and not more than 14 mL, and the number of cells loaded onto the gradient is at least 50 million but does not exceed 100 million; v) forced through the gradient by centrifugation at 800× G for 20-30 minutes with no brake; and segmented at a density between 1.063 g/mL and about 1.091 g/mL; and/or is characterized by a marker selected from the group consisting of VEGF, KDR, HIF1a, Podocin (Podn) or Nephrin (Neph), chemokine (C—X—C motif) receptor 4 (Cxcr4), endothelin receptor type B (Ednrb), collagen, type V, alpha 2 (Col5a2), Cadherin 5 (Cdh5), plasminogen activator, tissue (Plat), angiopoietin 2 (Angpt2), kinase insert domain protein receptor (Kdr), secreted protein, acidic, cysteine-rich (osteonectin) (Sparc), serglycin (Srgn), TIMP metallopeptidase inhibitor 3 (Timp3), Wilms tumor 1 (Wt1), wingless-type MMTV integration site family, member 4 (Wnt4), regulator of G-protein signaling 4 (Rgs4), Platelet endothelial cell adhesion molecule (Pecam), and Erythropoietin (Epo); and/or is capable of stabilizing, reducing the decline, or improving one or more renal functions in an immunocompatible subject that has renal disease.

[0031] In one aspect, the present invention provides isolated populations of erythropoietin (EPO)-producing kidney cells. In one embodiment, the population is an isolated, enriched population of EPO-producing mammalian cells. In another embodiment, the population is an isolated, enriched population of erythropoietin (EPO)-producing mammalian cells comprising a greater proportion of EPO-producing cells than a non-enriched population containing erythropoietin (EPO)-producing mammalian cells.

[0032] The population may be derived from a kidney tissue or cultured kidney cells. The population may be derived from a kidney sample obtained from a subject. The sample may be kidney tissue or cultured kidney cells derived from a kidney sample obtained from a subject. In another embodiment, the cell populations contain a greater proportion of EPO-producing cells than a non-enriched population containing EPO-producing mammalian cells. In one other embodiment, the cell populations contain a lesser proportion of renal tubular cells than a non-enriched population containing erythropoietin (EPO)-producing mammalian cells.

[0033] In all embodiments, the cell populations may be enriched for EPO-producing cells. In all embodiments, the cell populations may be enriched for non-EPO-producing cells. In all embodiments, the cell populations may be enriched for renal tubular cells.

[0034] In another aspect, the present invention provides cell populations of erythropoietin (EPO)-producing cells that are bio-responsive under certain culturing conditions. In one other embodiment, the bio-responsiveness is the induction of EPO expression when the cell population is cultured under hypoxic conditions when compared to a cell population cultured under non-hypoxic conditions. In yet another embodiment, the bio-responsiveness is an increase in EPO expression when the cell population is cultured under hypoxic conditions when compared to a cell population cultured under non-hypoxic conditions. In some embodiments, the hypoxic culture conditions include, without limitation, subjecting a cell population to a reduction in available oxygen levels in the culture system relative to a cell population cultured under conditions where the oxygen level is not reduced. In one other embodiment, the reduction in available oxygen levels is about less than 5% and the conditions where oxygen levels are not reduced is atmospheric oxygen levels (about 21%). In another embodiment, an increase in expression of EPO may be observed at oxygen levels less than atmospheric (21%) when compared to cultures tested at levels≧21%. In another embodiment, the induction of EPO expression and/or the increased EPO expression may be observed upon culturing cells in about less than 5% oxygen, i.e., hypoxic culture conditions, and comparing the level of induction and/or increased expression to cells cultured at atmospheric oxygen levels (about 21%), i.e., non-hypoxic culture conditions. In one embodiment, the EPO expression that is bio-responsive to hypoxic conditions is regulated by hypoxia inducible factor HIF. In another embodiment, the EPO expression that is bio-responsive to hypoxic conditions is regulated by HIF1α. In yet another embodiment, the EPO expression that is bio-responsive to hypoxic conditions is regulated by hypoxia inducible factor HIF2α.

[0035] In one embodiment, the bio-responsiveness is the induction of EPO expression when the cell population is cultured via perfusion when compared to a cell population not cultured via perfusion. In another embodiment, the bio-responsiveness is an increase in the expression of EPO when compared to a cell population not cultured via perfusion. In some embodiments, the perfusion conditions include, without limitation, transient, intermittent or continuous circulation or agitation of fluid such that dynamic forces are transferred to the cells via the flow of fluid. In another embodiment, the perfusion culture conditions are carried such that the cell populations are cultured in or on a material that provides a framework and/or space that allows for the formation of three-dimensional structures.

[0036] In one other aspect, the present invention provides admixtures or combinations of kidney cells that contain the cell populations described herein. In one embodiment, the cell admixture includes a first cell population enriched for EPO-producing cells and a second cell population not enriched for EPO producing cells. In one other embodiment, the second cell population may contain one or more types of kidney-derived cells, which may include, without limitation, one or more of the following: tubular-derived cells, glomerulus-derived cells, interstitium-derived cells, collecting duct-derived cells, connective tissue-derived cells, blood-derived cells, or blood vessel-derived cells. In another embodiment, the second cell population is enriched for renal tubular cells.

[0037] In all embodiments, the renal tubular cells described herein may be characterized by expression of a tubular cell marker, which may include, without limitation, one or more of the following: Hyaluronic acid synthase 2 (HAS2), CYP2D25 (Vitamin D3 25-Hydroxylase), megalin, cubilin, N-cadherin, E-cadherin, Aquaporin-1, Aquaporin-2, RAB17, member RAS oncogene family (Rab17), GATA binding protein 3 (Gata3), FXYD domain-containing ion transport regulator 4 (Fxyd4), solute carrier family 9 (sodium/hydrogen exchanger), member 4 (S1c9a4), aldehyde dehydrogenase 3 family, member B1 (Aldh3b1), aldehyde dehydrogenase 1 family, member A3 (Aldh1a3), and Calpain-8 (Capn8)

[0038] In one aspect, the present invention provides isolated, enriched mammalian renal tubular cell populations. In one embodiment, the isolated cell population is enriched for renal tubular cells and contains at least some EPO-producing mammalian cells. In another embodiment, the cell population has a greater proportion of tubular cells than a non-enriched population containing tubular cells. In one other embodiment, the isolated, enriched population of mammalian renal